

AMENDMENTS

In the Specification:

Please insert the attached "Sequence Listing" as separately numbered pages 1-4 after the abstract.

Please replace paragraph [0173] with the following amended paragraph

[0173] A diagnostic kit may comprise methylation-specific and/or primers specific for unmethylated sequences. Examples of methylation-specific primer are 5'-TATATATTCGCGAGCGCGGTTT-3' (forward) (**SEQ ID NO:4**) and 5'-CGCTGCGCCCAGATGTT-3' (reverse) (**SEQ ID NO: 5**), corresponding to the SOCS-3 promoter region sequences -1005 to -983 and -754 to -737, respectively. Sequences of the unmethylation-specific primers were: 5'-TGTGGTGGT TGTTTATATATTTGTGAGTGTGGTT-3' (forward) (**SEQ ID NO: 6**) and 5'-CAACCAACAATAACCCAC ACTACACCCA -3' (reverse) (**SEQ ID NO:7**), corresponding to the SOCS-3 promoter region sequences -1018 to -984 and -748 to -720, respectively. Thus kits of the invention can comprises these primers or other primers that target the same CpG islands or other CpG islands that are methylated in cancer.

Please replace paragraph [0176] with the following amended paragraph

[0176] Total RNA from lung cancer cell lines, fresh lung cancer and paired adjacent normal tissue were isolated using TRIzol reagent (Life Technologies, Carlsbad, California). Poly (A) RNA of those samples were isolated further from the total RNA using Oligotex mRNA Kit (Qiagen Inc., Valencia, California). SOCS-3 cDNA insert from the cDNA construct in pCDNA3 vector was used as a probe for Northern blot. Northern blotting was carried out as described previously (26). The same membrane was then re-probed with a specific probe of L19 ribosomal protein as a standard. RT-PCR was performed in GeneAmp PCR system 9700 using One-step RT-PCR Kit from Life Technologies Inc., according to the manufacture's protocol. Primers for RT-PCR were obtained from Operon Technologies Inc. (Alameda, California). Primer sequences for a 579 bp fragment of the human SOCS-3 cDNA were: 5'-GTCACCCACAGCAAGTTTCC-3' (forward) (**SEQ ID NO: 8**) and 5'-

CCGACAGAGATGCTG AAGAG-3' (reverse) (**SEQ ID NO: 9**). A 395 bp fragment of a gene encoding the L19 ribosomal protein was used as an internal control.

Please replace paragraph [0178] with the following amended paragraph

[0178] Genomic DNA from the cell lines and fresh tissue samples was extracted using DNA STAT-60TM reagent (TEL-TEST, Inc., Friendswood, Texas), according to the manufacture's protocol. Bisulfite-modified genomic DNA was amplified using primers (5'-GTGTAGAGTAGTGATTAAATA-3' (forward) (**SEQ ID NO: 10**) and 5'-TCCTTAAACTAAACCCCTC-3' (reverse) (**SEQ ID NO: 11**) designed to amplify nucleotides -1084 to -671 of the SOCS-3 promoter region (the start codon ATG of SOCS-3 is defined as +1). The PCR products were cloned into TOPO-TA pCR2.1 vector (Life Technologies) and multiple randomly picked clones from each sample were sequenced using standard techniques.

Please replace paragraph [0179] with the following amended paragraph

[0179] Bisulfite-treated genomic DNA was amplified using either a methylation-specific or unmethylation-specific primer set. HotStarTaq DNA polymerase (Qiagen Inc.) was used in the experiments. Sequences of the methylation-specific primers were: 5'-TATATATTCGCG AGCGCGGTTT-3' (forward) (**SEQ ID NO: 12**) and 5'-CGCTGCGCCCAGATGTT-3' (reverse) (**SEQ ID NO: 13**), corresponding to the SOCS-3 promoter region sequences -1005 to -983 and -754 to -737, respectively. Sequences of the unmethylation-specific primers were: 5'-TGTGGTGGT TGTTTATATATTTGTGAGTGTGGTT-3' (forward) (**SEQ ID NO:14**) and 5'-CAACCAACAATAACCCAC ACTACACCCA -3' (reverse) (**SEQ ID NO: 15**), corresponding to the SOCS-3 promoter region sequences -1018 to -984 and -748 to -720, respectively.